

OX-40 (or CD134) expression is a member of the tumor necrosis factor receptor (TNFR) superfamily that binds to OX-40 ligand (OX-40L) expressed on antigen presenting cells, such as activated B-cells and dendritic cells. OX-40 expression is limited to activated CD4<sup>+</sup> T-cells. Co-stimulation of T-cells through OX-40 enhances T-cell proliferation and cytokine production. OX-40 has been suggested to play a role in sustaining proliferation of Th1 or Th2 effector cells and promoting the development of a Th2 response (Weinberg et al., 1998, *Seminars Immunology* 10: 471-480).

On page 3, please amend the paragraph beginning on line 24 as follows:

4-1BB ligand glycoprotein is a member of the TNFR superfamily that binds to a high affinity ligand (4-1BB ligand) expressed on antigen presenting cells (APCs), such as dendritic cells, macrophages and activated B-cells (Vinay et al., 1998, *Seminars Immunology* 10: 481-489). Expression of 4-1BB is restricted to primed CD4<sup>+</sup> and CD8<sup>+</sup> T-cells (Goodwin, R.G., et al., 1993, *Eur. J. Immunol.* 23: 2631-2641; Pollack, K.E., et al., 1993, *J. Immunol.* 150: 771-781) after antigen or mitogen induction. Its interaction with 4-1BB ligand provides a strong signal for expansion of TCR ligated T-cells. It has been shown that systematic administration of an agonistic monoclonal antibody causes tumor reduction in s.c. tumor bearing animals, and both CD4<sup>+</sup> and CD8<sup>+</sup> T-cells are involved in the anti-tumor response (Melero et al., 1997, *Nature Med.* 3: 682-685; Melero et al., 1998, *Eur. J. Immunol.* 28: 1116-1121). However, anti-4-1BB antibody treatment is not adequate to sustain long term immunity.

On page 7, please amend the paragraph beginning on line 14 as follows:

Figure 5. Subcutaneous challenge of long-term surviving animals after JC liver metastases treatment. Surviving (>120 days after tumor cell inoculation) animals after treatment with ADV/IL-12 or anti-4-1BB antibody alone, or the combination ADV/IL-12 + anti-4-1BB antibody or ADV/IL-12 + ADV/4-1BBL received a s.c. injection of JC parental cells or MCA26 cells. Formation of tumor was observed over a 4-week period. Naïve animals were also injected to assess the normal growth pattern of the 2 tumors. Various percentages of animals in the long-term surviving groups did not form any tumor. However, only the results of the ADV/IL-12 + ADV/4-1BBL group reached statistical significance compared to naïve controls for JC tumor growth (P=0.007, Fischer's exact test). Conversely, the rate of JC tumor growth was dramatically reduced among all surviving animals.